Citation:

Vessby B, Unsitupa M, Hermansen K, Riccardi G, Rivellese AA, Tapsell LC, Nälsén C, Berglund L, Louheranta A, Rasmussen BM, Calvert GD, Maffetone A, Pedersen E, Gustafsson IB, Storlien LH; KANWU Study. Substituting dietary saturated for monounsaturated fat impairs insulin sensitivity in healthy men and women: The KANWU Study. *Diabetologia.* 2001 Mar;44(3):312-9.

PubMed ID: 11317662

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- The primary aim was to conduct a study of adequate size and duration to examine whether a change of dietary fat quality affects insulin sensitivity in humans.
- The secondary aim was to investigate the possible effects of a change of fat quality on glucose-induced insulin secretion, as well as effect on serum lipids and lipoproteins and to see if the effects were influenced by addition of long chain n-3 fatty acids to the diet.

Inclusion Criteria:

- Five centers participated in the KANWU (Kuopio, Aarhus, Naples, Wollongong, and Uppsala) study.
- Participants were chosen at random for this study.
- Healthy men and women between the ages of 30-65 years with normal or moderately increased body weight (BMI of 22-32) were included.

Exclusion Criteria:

- Subjects with diabetes were excluded from this study.
- Subjects using lipid lowering drugs, thiazide diuretics, beta blockers and corticosteroids were excluded.

Description of Study Protocol:

Recruitment: Subjects were from the KANWU study. A five-center European study.

Design: Randomized controlled trial. Controlled dietary study (90 days) whereby participants were chosen at random for either the high SFA or MUFA diet. Within the groups there was a

second random assignment to supplements containing fish oil or a placebo capsule containing olive oil.

Blinding used (if applicable): The subjects did not know which diet they were on or which capsule they were taking (fish oil vs. olive oil).

Intervention (if applicable):

- 37% fat content (either high SFA or high MUFA) diet.
- Fish oil capsules or olive oil-placebo capsules.

Statistical Analysis

- Results for continuous variables are presented as mean and standard deviation
- Results of the analysis are presented as adjusted mean treatment effects within groups and their p values
- Differences between treatment groups for adjusted mean treatment effects are presented with p values and 95% confidence intervals

Data Collection Summary:

Timing of Measurements

- 90-day study, preceded by a 2-week stabilization period.
- Pretrial measurements were taken during the 2-week stabilization period.
- Tests and lab analysis were carried out during days -1 and 0 and repeated at days 89 and 90 (end of the diet period).
- Two additional 3-day dietary records were done at the beginning of the 2nd and 3rd month of the treatment period.

Dependent Variables

- Change in Insulin sensitivity
- Glucose tolerance
- Insulin concentrations
- Serum cholesterol and triglyceride tests, LDL-cholesterol testing, & apolipoprotein A-1 and B

Independent Variables

- Isoenergetic diets of high proportion of SFA diet or MUFA diet.
- Fish oil capsules vs. olive oil capsules

Control Variables

Description of Actual Data Sample:

Initial N: total of 162 adults: 86 males, 76 females

Attrition (final N): none; as above

Age: 30-65 years

Ethnicity: European adults

Other relevant demographics:

Anthropometrics BMI: average of 26 with a range of 22 to 32. Clinical characteristics of the subjects assigned at random to the different diets were similar.

Location: Five centers: Sweden, Italy, Finland, Denmark, and Australia.

Summary of Results:

Key Findings

- Insulin sensitivity was significantly impaired on the saturated fatty acid diet (-10%, P = 0.03) but did not change on the monounsaturated fatty acid diet (+2%, NS) (P = 0.05 for difference between diets).
- Insulin secretion was not affected.
- The addition of n-3 fatty acids influenced neither insulin sensitivity nor insulin secretion.
- The favourable effects of substituting a monounsaturated fatty acid diet for a saturated fatty acid diet on insulin sensitivity were only seen at a total fat intake below median (37% of energy).
- Here, insulin sensitivity was 12.5% lower and 8.8% higher on the saturated fatty acid diet and monounsaturated fatty acid diet respectively (P = 0.03)
- LDL cholesterol increased on the saturated fatty acid diet (+4.1%, P < 0.01) but decreased on the monounsaturated fatty acid diet (MUFA, -5.2%, P < 0.001), whereas lipoprotein (a) increased on a monounsaturated fatty acid diet by 12% (P < 0.001).

Effects of Treatment Diets on Insulin Sensitivity, Fasting Insulin, Peak Insulin Secretion and Blood Glucose Concentrations

	SAFA diet	MUFA diet	Mean difference in treatment effects SAFA - MUFA
Insulin Sensitivity Index (Si)	-10.3 %, P = 0.0318	+2.1%, P = 0.5175	-0.52 (95% CI: -1.09 to 0.04), P = 0.0534
Serum insulin (mU/l)	+3.5%, P = 0.4662	-5.8%, P = 0.0490	0.60 (95% CI: -0.40 to 1.60), P = 0.0582
First-phase insulin response (mU/l)	+9.0%, P = 0.0289	+10.1%, P = 0.1392	-0.50 (95% CI: -6.3 to 5.3), P = 0.6265
Plasma-glucose (mmol/l)	0.0%, P = 0.9950	-0.6%, P = 0.4126	0.03 (95% CI: -0.07 to 0.14), P = 0.5572

Author Conclusion:

A change of the proportions of dietary fatty acids (decreased SFA and increased MUFA) improves insulin sensitivity, but has no effect on insulin secretion. A beneficial impact of the fat quality on insulin sensitivity is not seen in individuals with a high fat intake (>37% of energy).

Reviewer Comments:

Large sample size.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes

3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	???
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	???
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A

5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes

8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes